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CELEBRATING OUTSTANDING SCIENCE AT
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Imsidolimab, an Anti-IL-36 Receptor Monoclonal Antibody, in the Treatment of Generalized Pustular Psoriasis: Results from a Phase 2 Trial

Saturday October 2, 2021

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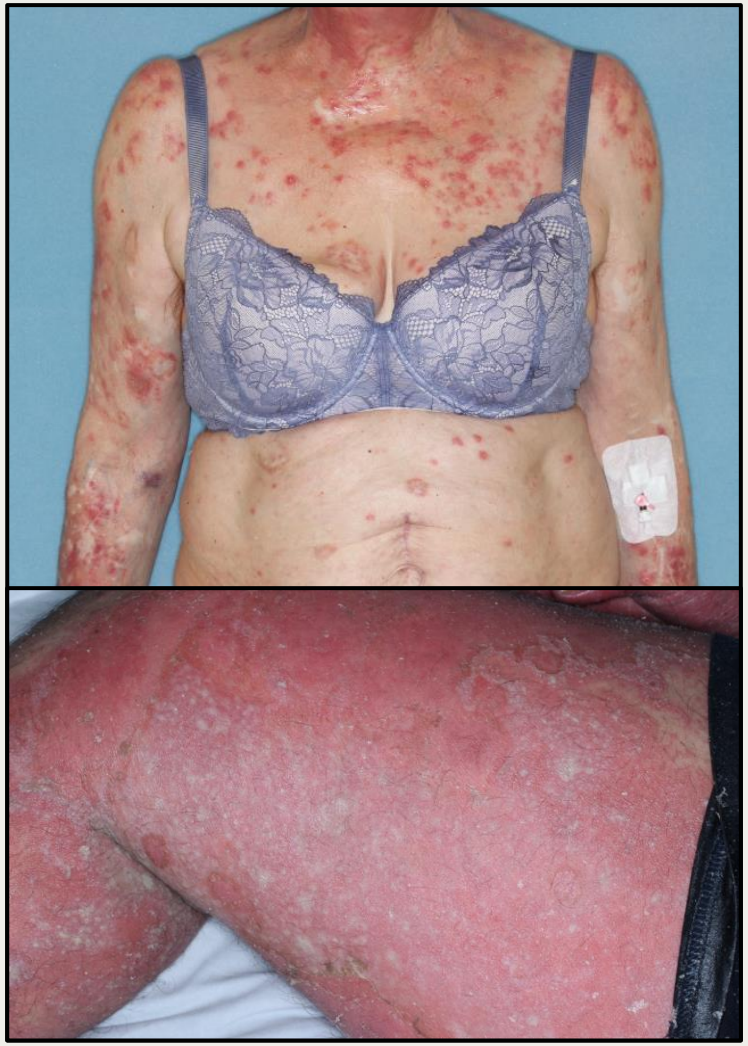
Generalized Pustular Psoriasis

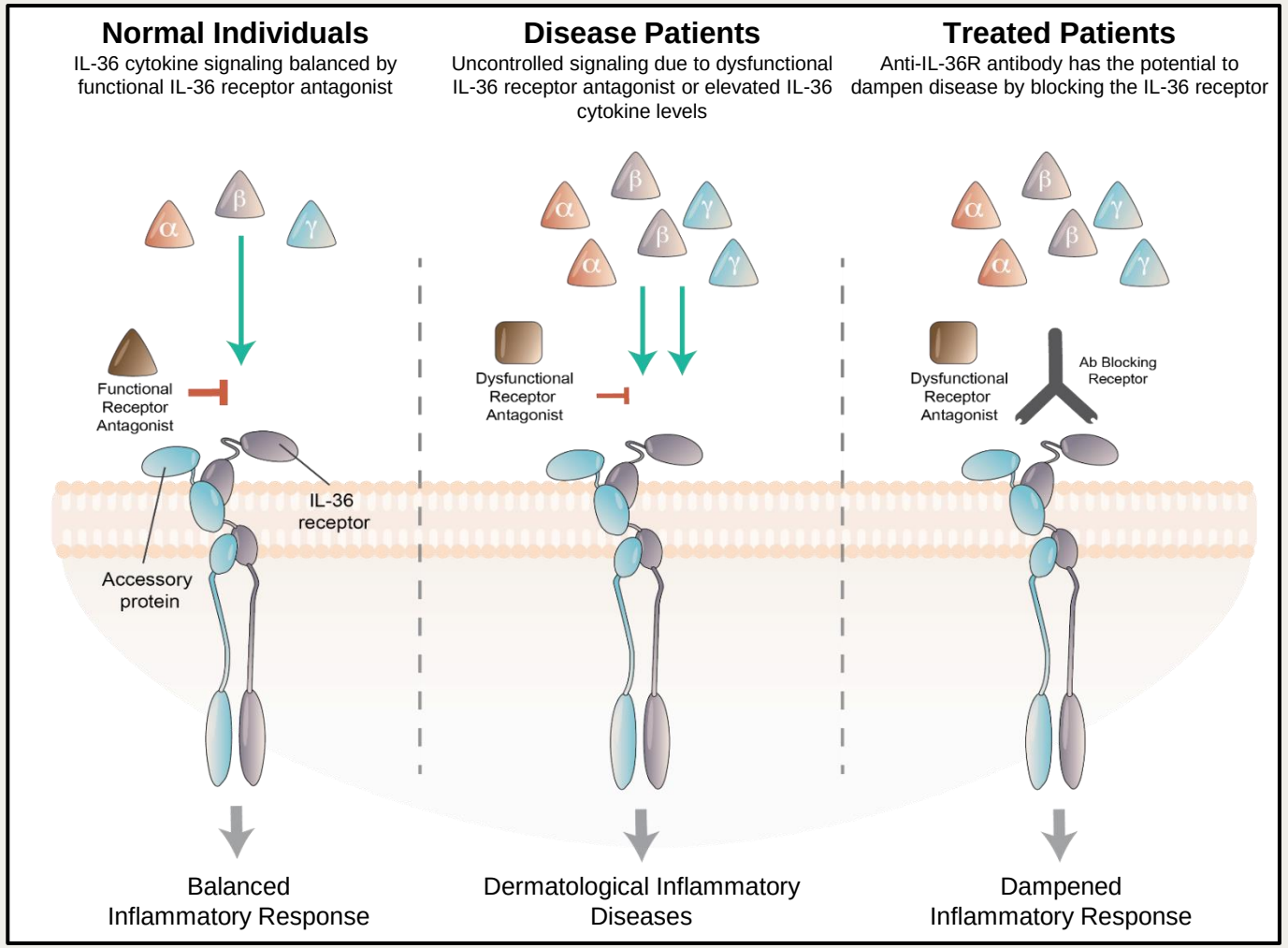
- A rare, life-threatening, inflammatory disease[1]
  - Recurrent flares of erythematous, pustular rash
  - Fever, general malaise, hyperleukocytosis, and elevated C-reactive protein
- Clear evidence of IL-36 axis involvement in GPP pathogenesis[2]
  - Mutations in *IL36RN*, *CARD14*, *AP1S3*, *TNIP1*, and *SERPINA3* predispose individuals to GPP
  - Dysregulated activation of IL-36R pro-inflammatory signaling cascade
- No approved therapies for GPP in US and EU
  - SOC is off-label use of systemic immunomodulators with potentially meaningful safety risks
  - Need for new, safe, and rapidly effective medicines



[1]Gooderham et al. *Exp Rev Clin Immunol* 2019;15:907-919; [2]Uppala et al. *Cell Mol Immunol* 2021;18:307-317; Images: AnaptysBio, data on file; *AP1S3*, adapter protein complex 1 subunit sigma 3 gene; *CARD14*, caspase recruitment domain-containing protein 14 gene; *IL36RN*, interleukin 36 receptor antagonist gene; *SERPINA3*, serine protease inhibitor gene serpin family A member 3; SOC, standard of care; *TNIP1*, TNFAIP3-interaction protein 1.

Imsidolimab

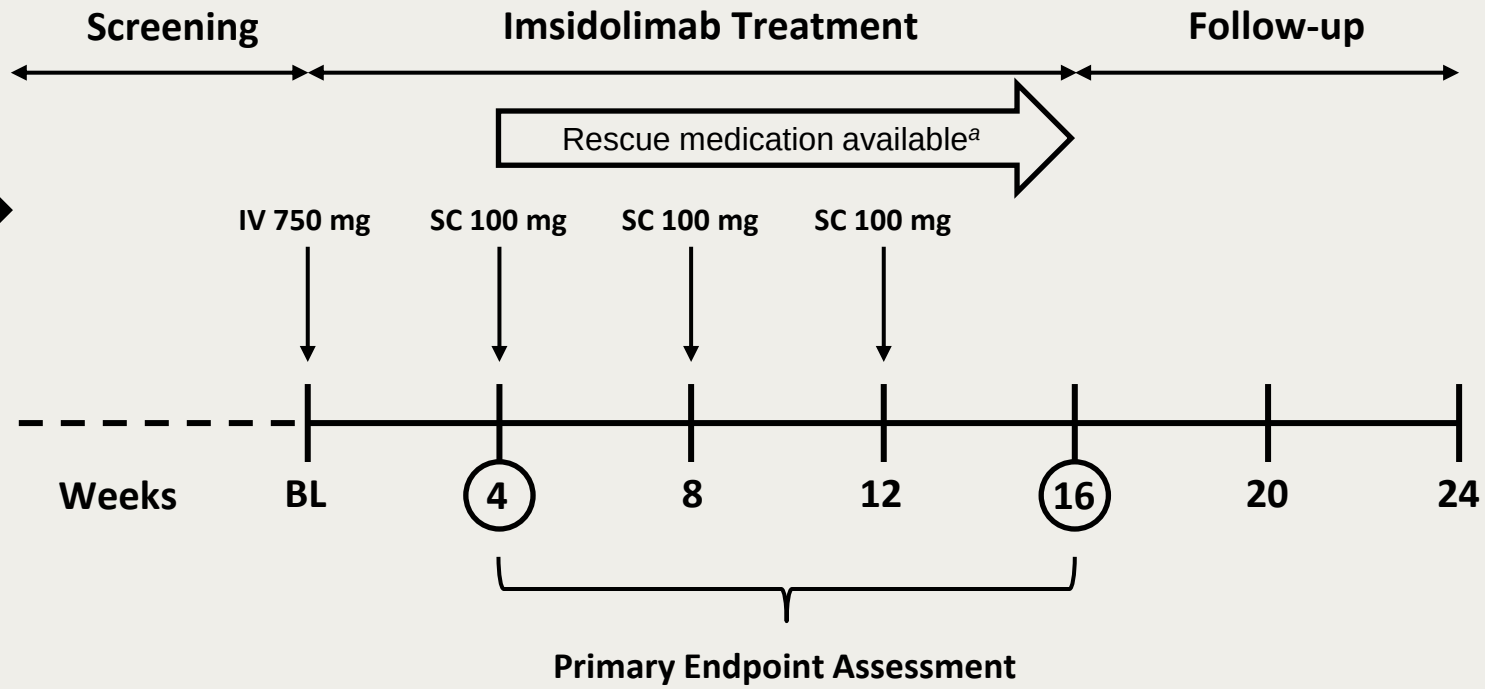
- Imsidolimab (ANB019) is an investigational humanized anti-IL-36R monoclonal antibody that antagonizes IL-36 cytokine pro-inflammatory signaling



GALLOP Phase 2 Study Design

Subjects with moderate-to-severe GPP flare:

- mJDA-SI >6
- BSA of erythema with pustules ≥10%



The primary efficacy endpoint was the proportion of subjects with improvement in Clinical Global Impression (CGI) based on the modified Japanese Dermatology Association Severity Index (mJDA-SI) at Week 4 and Week 16 with imsidolimab monotherapy

[a]Rescue medication used at the discretion of the Investigator and delayed, if possible, for at least 1 month following administration of study treatment. The use of any systemic psoriasis medication likely to impact psoriasis signs and symptoms requires subject withdrawal from the study; BL, baseline; BSA, body surface area; CGI improvement defined as "Very Much", "Much", or "Minimally" improved; IV, intravenous; SC, subcutaneous; NCT03619902.

Subject Baseline Characteristics

Characteristic	Safety Population (N=8)
Age (years), mean (SD)	51.3 (14.91)
Female gender, n (%)	4 (50.0)
Not Hispanic or Latino Ethnicity, n (%)	8 (100.0)
White Race, n (%)	7 (87.5)
BMI (kg/m^2), mean (SD)	28.86 (3.417)
mJDA-SI (range: 1-17) Total score, mean (SD) Moderate or Severe Severity, n (%)	 9.1 (2.75) 7 (87.5)
Area of erythema with pustules (% BSA), mean (SD)	23.51 (18.151)

BMI, Body Mass Index; BSA, body surface area; mJDA-SI, modified Japanese Dermatology Association Severity Index [total score categorization: 1-6 (mild); 7-10 (moderate); 11-17 (severe)]; SD, standard deviation.

Seventy-Five Percent of Subjects were CGI Responders at Weeks 4 and 16

CGI Responder Status[a]	Week 4	Week 16
Responder, n (%)		
Very Much Improved	4 (50.0)	4 (50.0)
Much Improved	2 (25.0)	1 (12.5)
Minimally Improved	0 (0.0)	1 (12.5)
Total, n (%) (95% CI)	**6 (75.0) (34.91, 96.81)**	**6 (75.0) (34.91, 96.81)**
Non-Responder, n (%)		
No Change	0 (0.0)	0 (0.0)
Worsened	0 (0.0)	0 (0.0)
Missing[b]	2 (25.0)	2 (25.0)
Total, n (%) (95% CI)	2 (25.0) (3.19, 65.09)	2 (25.0) (3.19, 65.09)
Total, n (%)	8 (100.0)	8 (100.0)

[a]Clinical response based on the Clinical Global Impression (CGI) scale per the modified Japanese Dermatology Association Severity Index (mJDA-SI) score; [b]Missing responder status, regardless of reason, was categorized as non-responder. Two subjects discontinued the study prior to Week 4: use of prohibited medication (infliximab, Day 15 Visit; discontinued from study on Day 22) (n=1) and lack of efficacy (Day 22) (n=1); CI, confidence interval.

- None of the 6 subjects evaluated at Weeks 4 and 16 required rescue medication during the treatment period

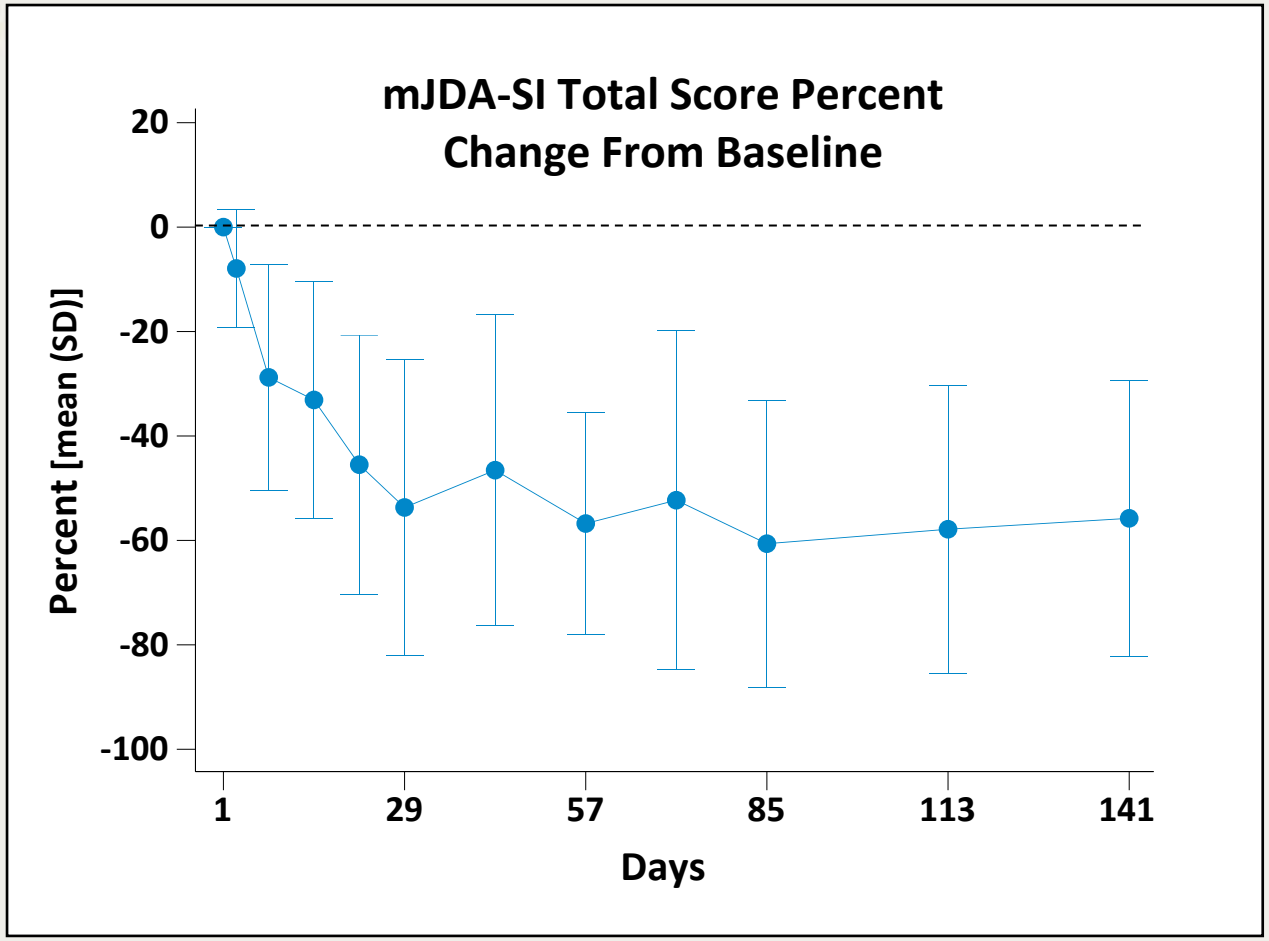
Fifty and Seventy-Five Percent of Subjects were GPPPGA *Clear* or *Almost Clear* at Weeks 4 and 16, Respectively

GPPPGA Responder Status[a]	Week 4	Week 16
Responder, n (%)		
0 (Clear)	0 (0.0)	1 (25.0)
1 (Almost Clear)	2 (50.0)	2 (50.0)
Total, n (%) (95% CI)	**2 (50.0) (6.76, 93.24)**	**3 (75.0) (19.41, 99.37)**
Non-Responder, n (%)		
2 (Mild)	2 (50.0)	1 (25.0)
3 (Moderate)	0 (0.0)	0 (0.0)
4 (Severe)	0 (0.0)	0 (0.0)
Total, n (%) (95% CI)	2 (50.0) (6.76, 93.24)	1 (25.0) (0.63, 80.59)
Total, n (%)	4 (100.0)	4 (100.0)

[a]Clinical response based on the GPP Physician Global Assessment (GPPPGA) scale; CI, confidence interval.

- The GPPPGA was implemented by protocol amendment after study start and only 4 subjects had assessments at Baseline, Week 4, and Week 16

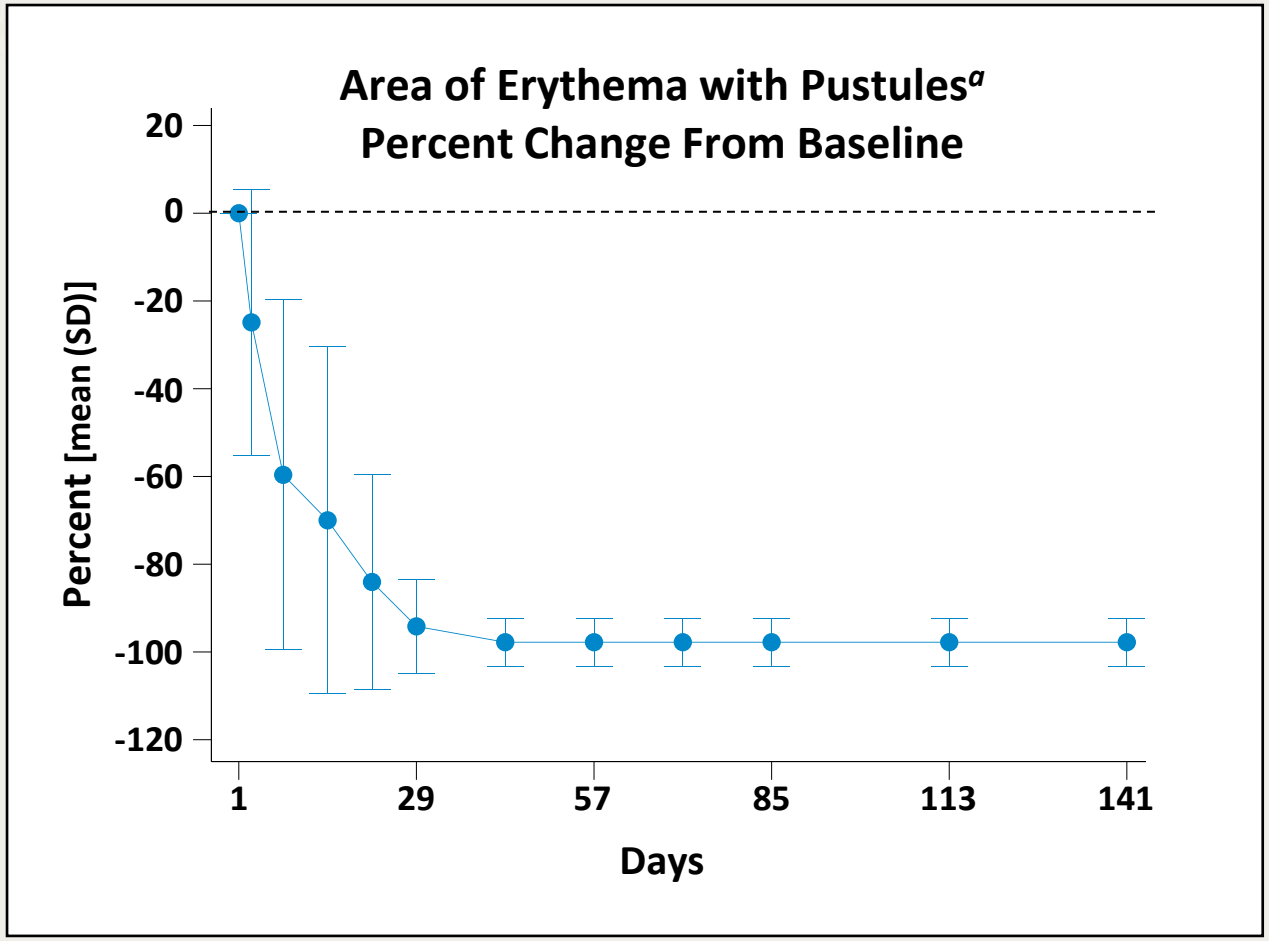
Subjects Experienced Rapid and Sustained Improvement in GPP Disease Signs and Symptoms



Time Post-Baseline	% CFBL (SD)
Day 3	-7.92 (11.330)
Week 1 (Day 8)	-28.78 (21.604)
Week 4 (Day 29)	-53.69 (28.374)
Week 16 (Day 113)	-57.86 (27.590)

mJDA-SI; modified Japanese Dermatology Association Severity Index; mJDA-SI Total Score is the sum of the mJDA-SI total skin lesions score and the total systemic manifestations score; %CFBL, percent change from baseline; SD, standard deviation.

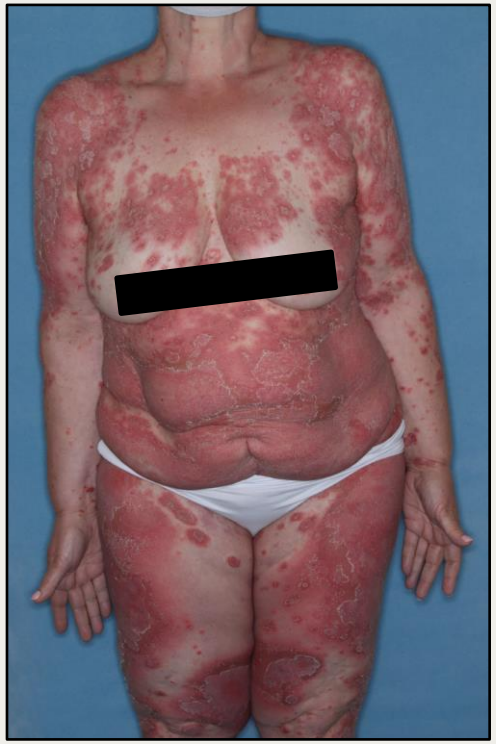
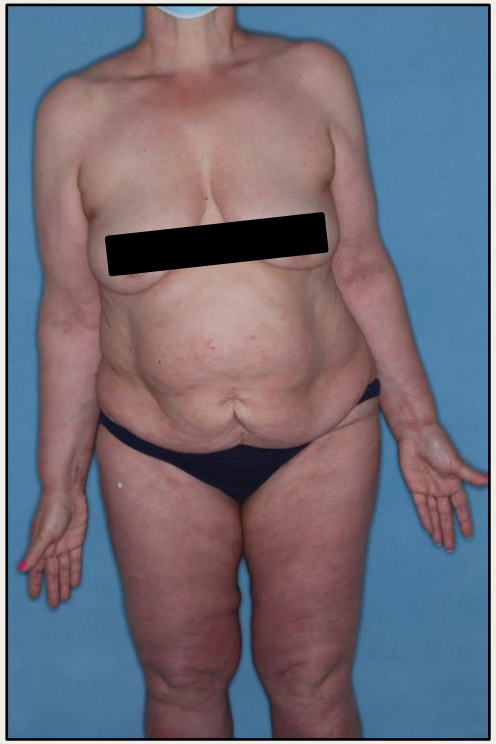
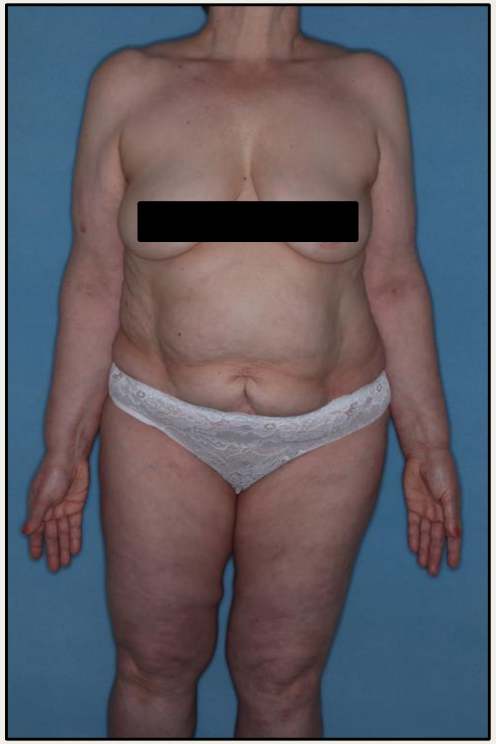
Subjects Experienced Rapid and Sustained Reduction of Area of Erythema with Pustules



Time Post-Baseline	% CFBL (SD)
Day 3	-24.88 (30.354)
Week 1 (Day 8)	-59.63 (39.895)
Week 4 (Day 29)	-94.17 (10.737)
Week 16 (Day 113)	-97.78 (5.443)

[a]Area of erythema with pustules is the percent body surface area (BSA) of erythema with pustules; %CFBL, percent change from baseline; SD, standard deviation.

Subject Photographic Evidence Consistent with Investigator Assessments of GPP Disease Severity

	Baseline	Week 4	Week 16
			
CGI	**N/A**	***Very Much Improved***	***Very Much Improved***
Area E/P	**30**	**0**	**0**
GPPPGA	**4**	**1**	**1**

Area E/P, percent body surface area of erythema with pustules; CGI, Clinician Global Impression scale; GPPPGA, GPP Physician Global Assessment scale.

Subjects Experienced Clinically Meaningful Reduction in DLQI Total Score

Dermatology Life Quality Index	Imsidolimab (N=8)		
	Total Score	CFBL[a]	% CFBL
Baseline (n=8) Mean (SD)	15.8 (9.62)		
Week 1 (n=8) Mean (SD)	14.9 (10.22)	-0.9 (3.56)	-7.69 (28.821)
Week 4 (n=6) Mean (SD)	**11.7 (7.23)**	**-6.0 (9.08)**	**-28.46 (31.279)**
Week 16 (n=6) Mean (SD)	7.0 (3.52)	-10.7 (9.16)	-55.19 (27.426)

[a]CFBL, change from baseline.

- A reduction in DLQI Total Score of 4 points is considered a minimal clinically important difference (MCID) in inflammatory skin conditions[1]

Safety and Tolerability Summary

- Imsidolimab was generally well-tolerated and associated with acceptable safety in this Phase 2 study of subjects with active GPP
  - 3/8 (37.5%) subjects reported 5 TEAEs related or possibly related to study treatment:
    - Nausea (moderate), nosocomial infection (severe), oropharyngeal pain (mild), psoriasis (moderate), and vomiting (moderate)
  - 2/8 (25.0%) subjects had serious AEs (SAEs) and recovered without sequelae
    - Severe sepsis due to nosocomial infection on Day 7
      - Subject received prohibited medication (infliximab) on Day 15 Visit and discontinued from study on Day 22
    - Mild SARS-CoV-2 infection
      - Subject experienced interruption of study drug treatment, completed study, and was a responder
  - No subject discontinued the study due to a TEAE
  - No infusion-related TEAEs or injection site reactions

Phase 2 Study of Imsidolimab in the Treatment of GPP Summary and Conclusions

- This was a Phase 2 open-label, single-arm, multiple-dose clinical trial of imsidolimab monotherapy in subjects with active moderate-to-severe GPP
- Most subjects experienced rapid, sustained, and clinically meaningful improvements in disease severity across multiple complementary efficacy measures
- Imsidolimab was generally well-tolerated and the majority of TEAEs were mild-to-moderate in severity
- Antagonism of the IL-36 pro-inflammatory signaling axis with imsidolimab represents a novel therapeutic strategy for addressing this potentially life-threatening disease with no approved treatments
- These data strongly support continued development of imsidolimab in GPP subjects experiencing flare
- Phase 3 studies are currently being planned

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